

REMARKS

Reconsideration of the rejections set forth in the Office action mailed April 8, 2004 is respectfully requested. Claims 1-6, 9-10 and 12-13 are currently pending in this reissue application.

I. Current Amendments

Claim 5 is amended to replace "a thousand or more" with "from ten thousand to a hundred thousand". Support is found in the specification at column 16, lines 51-53 of U.S. Patent No. 5,654,413 (hereinafter "the '413 patent"). Claim 8 is accordingly cancelled.

Claim 9 (which was not subject to the 103(a) rejection in this Office Action) has been redrafted in independent form, incorporating all the limitations of previous claim 5.

Claim 11 is cancelled, and claim 13 is amended to correct a typographical error.

No new matter is added by any of the amendments.

II. Specification

Enclosed is a substitute specification including the claims, in accordance with 37 CFR §1.173, as requested.

The claims are presented in their currently pending form, as amended, relative to the patent specification in effect as of the date of filing of the reissue application (in accordance with MPEP §1453).

The claims as presented incorporate the following amendments:

- Claims 5-13 were filed as new in the reissue application on August 2, 1999.
- Claims 5-6 and 8-9 were amended (albeit in improper format), and claim 7 was cancelled, in a response filed May 7, 2000. (It is noted that the same amendments were presented in a response filed on January 4, 2001, and in a CPA application filed on February 10, 2001. The claims were marked "Twice amended" even though no new amendments were presented.)
- Claim 5 was further amended (albeit in improper format) in a response filed by the undersigned on December 9, 2001.

- Claims 5, 9 and 13 are amended, and claims 8 and 11 are cancelled, with this response.

The specification as presented incorporates only the amendment to the paragraph at column 15, lines 51-65, presented in the response filed May 7, 2000.

The specification as presented does not incorporate the amendments (concerning the Sequence Listing) presented in the response and CPA filed on January 4, 2001 and February 10, 2001, respectively. In view of the complexities that have arisen regarding changes to the Sequence Listing, applicant requests that these amendments be retracted, and that the original Sequence Listing in the '413 patent be retained.

III. Drawings

Enclosed are copies of drawing sheets 1-6 from the '413 patent, with the header information removed, as required by the Draftsperson's drawing review mailed with the Office Action of April 25, 2000.

IV. Sequence Listing

As noted above in Section II, in view of the complexities that have arisen regarding changes to the Sequence Listing, applicant requests that the amendments concerning the Sequence Listing presented in the response and CPA filed on January 4, 2001 and February 10, 2001, respectively, be retracted, and that the original Sequence Listing in the '413 patent be retained. (Applicant notes that the amendments regarding the Sequence Listing presented in the response filed June 20, 2002 were not entered, as stated on page 3 of the current Office Action.)

V. Rejections under 35 USC §251: Reissue Oath/Declaration

Claims 1-6 and 8-13 were rejected under 35 USC §251 as being based upon a defective reissue declaration. The Examiner contended that no specific error in the prosecution of the '413 patent, to be relied upon as a basis for reexamination, was identified.

The Examiner stated that receipt of an appropriate supplemental declaration would

overcome the rejection.

Although the applicant believes that a specific error was in fact identified in the Declaration filed on May 17, 2000, a signed Supplemental Reissue Application Declaration which more clearly identifies the error is enclosed. (A duplicate, unsigned copy of the signature page is also enclosed.)

VI. Rejections under 35 USC §251: Recapture

Claims 10-13 were rejected under 35 USC §251 as directed to an improper recapture of broadened claimed subject matter surrendered in the application for the patent upon which the reissue is based. The Examiner stated that the broadening aspect of these claims was surrendered by the applicant during the prosecution of the '413 patent, in view of the Examiner's description of Allowable Subject Matter in the prosecution of that patent.

In the prosecution of the '413 patent, the Examiner's description of Allowable Subject Matter, in the Office Action dated March 19, 1996, discussed the teachings of two cited references, Chetverin *et al.* and Brenner *et al.* The Examiner in the '413 patent stated that:

...The reference [Chetverin *et al.*] does not teach or suggest attaching oligonucleotide tags to the polynucleotides and sorting on the sole basis of the attached "hybridization tag" by hybridization to the tag complement....The reference [Brenner *et al.*] does not suggest increasing the minimum number of mismatches between a given tag and incorrect tag complements to at least two mismatches, i.e. subunits chosen from a minimal cross-hybridizing set..., nor using such tags to sort polynucleotides. There is no clear motivation in either Chetverin *et al.* or Brenner *et al.* that would lead one of ordinary skill in the art to combine the teachings of the two references to arrive at the claimed invention. [emphasis added]

The present Examiner refers to the "minimum number of mismatches between a given tag and incorrect tag complements" as "the specific element the Examiner [in the '413 patent] said was necessary to be free of the prior art" (page 8 of present Office Action).

However, as is clear from the passage quoted above, this element was not the only element that the '413 Examiner found was not suggested by the prior art. For example, the '413 Examiner also stated that the Brenner reference did not teach "using such tags to sort polynucleotides".

The MPEP states that "The argument that the claim limitation defined over the rejection must have been specific as to the limitation relied upon" (§1412.02(I)(B)(2); page 1400-16). In this case, the finding of allowability over the Brenner and Chetverin references did not rely solely on the limitation reciting a number of mismatches. Accordingly, the '413 Examiner's statement does not constitute a clear surrender of this subject matter.

VII. Format of Previous Amendments

The Examiner noted that previous amendments to the claims had been entered in a format which was improper for a reissue application; that is, with changes indicated relative to the previous version of the claims, rather than to the issued '413 patent.

The substitute specification, including claims, which is enclosed herein includes the pending claims with changes indicated relative to the patent specification in effect as of the date of filing of the reissue application, in accordance with MPEP §1453. Changes are indicated by underlining of added material, i.e., the entire text of each of claims 5-13, with the exception of claim 7, which was cancelled in the amendment submitted on February 10, 2001, and claim 8, which is cancelled with this response.

Marked up copies of the amended claims relative to the prior pending versions were provided in the amendments submitted on February 10, 2001 and December 9, 2001.

Enclosed herewith, on pages 2-3 of this communication, is a marked up copy of claims 5, 9 and 13, as currently amended, relative to the previous version of these claims.

VIII. Rejections under 35 USC §112, first paragraph and 35 USC §251: Written Description/New Matter

Claim 5 and its dependent claims 6, 8, and 9 were rejected under 35 USC §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the

application was filed, had possession of the claimed invention.

The same claims were rejected under 35 USC §251 as being based upon new matter added to the patent for which reissue is sought.

Independent claim 5 has been amended to change "a thousand or more" to "from ten thousand to a hundred thousand", in reference to the number of different polynucleotides comprised by the claimed composition. Explicit support is found, for example, at column 16, lines 51-53 of the '413 patent.

IX. Rejections under 35 U.S.C. §103

Independent claim 5 and dependent claims 6 and 8 were rejected under 35 U.S.C. §103(a) as being unpatentable over Wang *et al.* (EP 0304845) in view of Hornes *et al.* (U.S. Patent No. 5,512,439). The rejections are respectfully traversed in light of the following remarks.

A. The Invention

The applicant's invention, as embodied in independent claim 5, is directed to a composition of matter comprising a plurality of from ten thousand to a hundred thousand different polynucleotides, selected from cDNA molecules or fragments of a target polynucleotide. The composition includes a mixture of microparticles, wherein each microparticle has polynucleotides of the plurality attached thereto, and wherein substantially all different polynucleotides in the plurality are attached to different microparticles.

B. Analysis

In the reiterated rejection, as set forth in this Office Action, the Examiner fails to distinguish between the number of molecules of a polynucleotide that can be attached to a single microparticle (i.e., in the Examiner's discussion of cited reference Hornes *et al.*) and the number of different polynucleotides comprised by the applicant's claimed composition, where "substantially all different polynucleotides are attached to different microparticles".

For example, in response to applicant's earlier statement that "neither Wang *et al.* nor Hornes *et al.* teach [that] the *different polynucleotides* number a thousand or more" (emphasis added), the Examiner counters that "Hornes *et al.* does teach" that "each magnetic particle carries $10^3 - 10^6$ probes" (page 11 of Office Action). However, the number of

probe molecules attached to "each magnetic particle" in Hornes *et al.* has nothing to do with the number of different polynucleotides that are represented in the microparticle composition claimed by the applicant. That is, a composition in which "each magnetic particle carries 10^3 – 10^6 probes", as stated in Hornes, could comprise any number of particles (even a single particle) having 10^3 – 10^6 copies of the same molecule (such as oligo-T) attached. On the contrary, the applicant's claimed composition includes at least ten thousand microparticles, each containing a different polynucleotide.

The Examiner further states that Hornes *et al.* "is relied on to teach the advantages of attaching a plurality of oligonucleotides, numbering 10^3 – 10^6 , to microbeads" (page 12 of Office Action). Because independent claim 5 includes no limitation as to the number of oligonucleotides on a microbead, this teaching does not appear to be pertinent to claim 5.

With respect to Wang *et al.*, the Examiner further states that "Wang *et al.* is relied upon to teach applications wherein different probes are attached to microparticles". In the previous response, the applicant stated that the procedures taught by Wang *et al.* employ, at most, "several" different types of probe molecules attached to labeled microparticles. The Examiner replies that Wang teaches "applications where it would be advantageous to have a thousand or more probes".

However, even if it would be "advantageous" to provide "a thousand or more probes", the cited art does not teach or suggest how one would make or use a composition comprising thousands of different probes, each on a different microparticle. "In order to render a claimed apparatus or method obvious, the prior art must enable one skilled in the art to make and use the apparatus or method." *Beckmann Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547, 13 USPQ2d 1301 (Fed. Cir. 1989), quoted in *Motorola, Inc. v. Interdigital Technology Corp.*, 121 F.3d 1461, 43 USPQ2d 1481 (Fed. Cir. 1997) and *Rockwell International Corp. v. United States*, 147 F.3d 1358, 47 USPQ2d 1027 (Fed. Cir. 1998).

Moreover, in Wang's discussion of assays employing different probes, it is necessary that microparticles having different probes are distinctly labeled (e.g., "several assays can be performed in a single procedure by using several corresponding trace elements"; "the differently labeled microbeads can be separately detected"; page 4, lines 47-56). There is no teaching of how one would supply thousands of distinct labels to label thousands of different

probes. As described in the passage cited above, the distinct labels in Wang *et al.* are preferably different heavy metal atoms, of which there is a limited supply. Accordingly, one skilled in the art would not envision the use of thousands of different probes from the teachings of Wang *et al.*

As explained above, Wang *et al.* and Hornes *et al.* in combination do not suggest the applicant's composition, nor do they teach how such a composition could be prepared.

In view of the foregoing, the applicant respectfully requests the Examiner to withdraw the rejection under 35 U.S.C. §103(a).

X. Conclusion

In view of the foregoing, the applicant submits that the claims now pending are now in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4403.

Respectfully submitted,



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